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Effect of COVID-19 infection on the auditory pathway to the brainstem

Efeito da infecção por COVID-19 na via auditiva até tronco encefálico

Efecto de la infección por COVID-19 en la vía auditiva hacia el tronco del encéfalo

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Abstract

Introduction: COVID-19 can affect the auditory system, justifying the evaluation of the hearing of infected individuals. **Objective:** to analyze the auditory pathway to the brainstem of individuals affected by COVID-19 compared to the control group. **Method:** Analytical cross-sectional observational study carried out in a non-probabilistic sample of adults who had COVID-19, who were compared with a control group, without hearing complaints. The evaluation consisted of: acoustic immittance measurements, pure tone audiometry (PTA), transient stimulus-evoked otoacoustic emissions (TEOAE) and brainstem auditory evoked potential (BAEP). **Results:** 77 individuals were evaluated, 41 participants in the COVID-19 group (average age of 26.3) and 36 in the control group (average age of 25.8). Hearing thresholds were within normal limits for all individuals in the COVID-19 group, being significantly higher for the frequencies of 1000, 2000 and 3000 Hz on the right. TEOAE amplitude was significantly lower in the 1500 frequency band on the right. There was a significant and negative correlation for the frequencies of 1000 Hz and 3000 Hz on the right and for the frequencies of 1000, 2000 and 3000 Hz on the left, between TEOAE and PTA. An increase in the absolute latency of wave I, of the BAEP, was observed in the left ear. **Conclusion:**

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Authors' contributions:
KK: developed the research, collected data, and wrote the manuscript.
EBP: collected data.
SMR: participated in manuscript review and editing.
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COVID-19 affected specific locations in the auditory system. There was a decrease in auditory acuity and the functioning of the outer hair cells of the cochlea, as well as an increase in the neural conduction time of sound in the distal portion of the VII cranial nerve on the left.

Keywords: COVID-19; Cross-Sectional Studies; Hearing; Adult, Hearing tests.

Resumo

Introdução: A COVID-19 pode afetar o sistema auditivo, justificando a avaliação da audição de indivíduos infectados. **Objetivo:** analisar a via auditiva até o tronco encefálico de indivíduos acometidos por COVID-19 comparados ao grupo controle. **Método**: Estudo observacional transversal analítico realizado em uma amostra não probabilística de adultos que tiveram COVID-19, que foram comparados com um grupo controle, sem queixa auditiva. A avaliação consistiu em: medidas de imitância acústica, audiometria tonal liminar (ATL), emissões otoacústicas evocadas por estímulo transiente (EOET) e potencial evocado auditivo de tronco encefálico (PEATE). **Resultados:** Foram avaliados 77 indivíduos, sendo, 41 participantes do grupo COVID-19 (idade média de 26,3) e 36 do grupo controle (idade média de 25,8). Os limiares auditivos estavam dentro dos padrões da normalidade para todos os indivíduos do grupo COVID-19, sendo significativamente maiores para as frequências de 1000, 2000 e 3000 Hz à direita. A amplitude das EOET foi significativamente menor na banda de frequência de 1500 à direita. Houve correlação significativa e negativa para as frequências de 1000 Hz e 3000 Hz à direita e para as frequências de 1000, 2000 e 3000 Hz à esquerda, entre EOET e ATL. Foi verificado aumento da latência absoluta da onda I, do PEATE, na orelha esquerda. **Conclusão**: a COVID-19 afetou locais específicos do sistema auditivo. Houve diminuição da acuidade auditiva e do funcionamento das células ciliadas externas da cóclea, bem como aumento do tempo de condução neural do som na porção distal do VII par craniano à esquerda.

Palavras-chave: COVID-19; Estudos Transversais; Audição; Adulto; Testes Auditivos.

Resumen

Introducción: COVID-19 puede afectar el sistema auditivo, justificando la evaluación de la audición de individuos infectados. **Objetivo:** analizar la vía auditiva hacia el tronco encefálico de individuos afectados por COVID-19 en comparación con el grupo control. **Método:** Estudio observacional analítico transversal realizado en una muestra no probabilística de adultos que padecieron COVID-19, quienes fueron comparados con un grupo control, sin escuchar quejas. La evaluación consistió en: mediciones de inmitancia acústica, audiometría de tonos puros (ATP), otoemisiones acústicas provocadas por estímulos transitorios (OAET) y potenciales evocados auditivos del tronco encefálico (PEATE). **Resultados:** Se evaluaron 77 individuos, 41 participantes en el grupo COVID-19 (edad promedio de 26,3 años) y 36 en el grupo control (edad promedio de 25,8 años). Los umbrales de audición estaban dentro de los límites normales para todos los individuos del grupo de COVID-19, siendo significativamente más altos para las frecuencias de 1000, 2000 y 3000 Hz de la derecha. La amplitud de OAET fue significativamente menor en la banda de frecuencia de 1500 de la derecha. Hubo correlación significativa y negativa para las frecuencias de 1000 Hz y 3000 Hz a la derecha y para las frecuencias de 1000, 2000 y 3000 Hz a la izquierda, entre OAET y ATP. Se observó un aumento de la latencia absoluta de la onda I, del PEATE, en el oído izquierdo. **Conclusión:** COVID-19 afectó ubicaciones específicas del sistema auditivo. Hubo una disminución de la agudeza auditiva y del funcionamiento de las células ciliadas externas de la cóclea, así como un aumento del tiempo de conducción neural del sonido en la porción distal del VII par craneal izquierdo.

Palabras clave: COVID-19; Estudios Transversales; Audición; Adulto; Pruebas Auditivas

Introduction

Hearing loss can result from various factors, including exposure to infectious diseases caused by bacteria, fungi, or viruses[1]. In the case of viral infections, different agents can cause hearing loss, resulting in varied manifestations and consequences[2]. These infections are responsible for approximately 3% of cases of sudden sensorineural hearing loss[1].

Furthermore, viral infections can affect both the middle ear, through infection of the upper airway, resulting in conductive hearing loss, and the inner ear, through viral invasion, damaging the cochlea and/or vestibulocochlear nerve[1]. The severity of hearing loss varies according to the affected location in the auditory structure, ranging from mild to profound[2].

Thus, the relationship between viral infections and hearing loss depends on the specific characteristics of each virus, whether it is congenital or acquired, and whether it affects unilaterally or bilaterally[1].

It is important to understand how SARS-CoV-2 infection affects the auditory system. Studies have indicated the influence of this virus in several ways, triggering a series of harmful changes that include inflammatory processes in the upper airways, which, consequently, can affect the middle ear, leading to symptoms of ear fullness, otalgia and decreased hearing acuity, the possibility of hypoxia in cochlear cells, due to decreased blood supply and symptoms such as sudden decrease in hearing, tinnitus and dizziness can be observed[3-5]. A meta-analysis study reported a 3.1% occurrence rate of hearing loss in adults confirmed with COVID-196. However, the authors emphasize the cautious interpretation of this result justified by the low level of evidence, such as studies carried out without a control group and the high heterogeneity between the articles included[6].

Therefore, carrying out studies that compare audiologically healthy individuals with those who had COVID-19, regardless of whether they had auditory and/or vestibular complaints, becomes essential for understanding the consequences of this disease on the auditory system[6,7].

Although some research has suggested a relationship between hearing acuity, tinnitus and vertigo and SARS-CoV-2 infection, current knowledge about the actual mechanisms and specific targets of the virus that cause these symptoms is still incipient[8].

The complexity of this issue lies in the multifaceted nature of COVID-19 infection and the interaction of the virus with different systems of the human body. It is also believed that the anatomical extensions of the virus to the middle ear may trigger an inflammatory response, or have a direct effect on the lining epithelium[6,7]. These interactions may result in temporary symptoms related to hearing and body balance during COVID-19[9].

However, it is important to highlight that understanding the mechanisms involved is an ongoing challenge. Furthermore, the variability of symptoms in individuals with COVID-19 and the lack of comprehensive data make it difficult to identify exact patterns of relationship between the virus and the auditory system.

Therefore, the search for knowledge about how SARS-CoV-2 affects hearing highlights the need for continued research and in-depth investigations. This effort is essential not only for a more complete understanding of the underlying mechanisms, but also for the development of more effective prevention and treatment strategies for affected individuals. The continuous expansion of our knowledge in this area is essential to improve the quality of health care and the recovery of those infected by the virus.

The objective of this study was to analyze the auditory pathway to the brainstem of individuals affected by COVID-19 compared to a control group.

Material and Method

This analytical cross-sectional observational study was carried out in a teaching clinic, assessing the COVID-19 group between November 2021 and October 2022 and the control group between January and November 2019.

The study was approved by the Human Research Ethics Committee (CAAE number 46189021.2.0000.0121), and all participants signed an informed consent form.

Sample

- COVID-19 group: Adults (aged 18 to 59 years) who had symptomatic COVID-19, whose diagnosis was confirmed with RT-PCR test (reverse transcription polymerase chain reaction), with no other comorbidities.
- Control group: Adults (aged 18 to 59 years) who attended the study site before the coronavirus pandemic, without any comorbidities or condi-

tions that could result in hearing loss, tinnitus, vertigo, or body balance problems.

To minimize possible confounding factors, individuals in the control group were evaluated before the start of the COVID-19 pandemic and individuals who had moderate or severe manifestations of the disease were not included in the study group.

The information obtained from the sample of the study group and the control group was extracted from the medical records of the research participants and all tests were carried out in a sound booth.

Exclusion criteria

The study excluded individuals with hearing complaints before COVID-19 infection in either ear, neurological deficits, cognitive impairment, and/or obstruction in the external auditory canal, unilaterally or bilaterally.

Research instruments

The research surveyed each participant's identification data, detailed medical history (including symptoms acquired after contamination), and otological and COVID-19 history, followed by an inspection of the external auditory meatus and an audiological evaluation.

The audiological evaluation comprised the following procedures:

- **Acoustic immittance measures:** the tympanometric curve and acoustic reflex were researched with AT235h equipment, Interacoustics, with 226-Hz tone probe. Tympanometry was performed automatically, applying variable pressure (+200 daPa to -300 daPa), a speed of 50 decapascals per second (daPa/s). The manual method was used in ipsilateral (dBSPL) and contralateral (dBHL) acoustic reflexes at 70 to 110 dB, at 500, 1000, 2000, and 4000 Hz.
- **Pure-tone threshold audiometry (PTA):** Conducted in a sound booth with an Otometrics audiometer, model MADSEN Astera, and SENNHEISER HDA 200 earphones. Pure-tone thresholds were researched bilaterally at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz through air-conduction. Individuals with air-conduction thresholds equal to or higher than 20 dBHL had their pure-tone thresholds researched through bone-conduction at 500 to 4000 Hz, using the B-71 bone transducer positioned on the mastoid. The descending method was used, and the threshold was defined as the lowest intensity at which 50% were identified[11].
- **Transient evoked otoacoustic emissions (TEOAE):** SmartEP equipment, IHS, with click stimuli at 1000 to 4000 Hz, at 80 dB, presentation rate of 19.30/s, totaling 3.048 stimuli, and with a maximum noise level of 48.47 dBSPL. For present responses the following were accepted: signal-to-noise ratio ≥ 3 dB, reproducibility ≥ 50%, and a minimum of 70% stability[12].
- **Auditory brainstem response (ABR):** SmartEP equipment, IHS, was used in a silent room, with the patient comfortably accommodated. After cleaning the skin with an abrasive substance (Nuprep®), the surface, active, and ground electrodes were fixed to the forehead (Fz, Fpz), and the reference electrodes were fixed to the earlobes (A1 and A2) (according to the 10/20 electrode positioning system). Filtered click stimuli were presented monaurally through ER 3A insert earphones (100-Hz high-pass filter and 3000-Hz low-pass filter), duration of 100 μs, and rarefied polarity. A total of 2.048 clicks were provided, with an analysis time of 20 ms, repeated to confirm the reproducibility of the waves. The impedance of the electrodes was always kept below 3 kilohms. The stimulus presentation rate was 21.1 clicks per second. Neural integrity was investigated with acoustic stimuli at 80 dBnHL. The analysis also addressed the absolute latencies of waves I, III, and V and interpeak intervals I – III, III – V, and I – V in both ears.

Data analysis

The initial descriptive analysis encompassed measures of central tendency (mean and median) and dispersion (standard deviation and percentiles). Inferential statistics were also performed, using the Mann-Whitney test to compare two independent samples without normal distribution and quantitatively analyze the results of all hearing tests (PTA, TEOAE, and ABR). The Spearman correlation test was applied to verify the relationship between TEOAE response amplitudes and PTA air-conduction hearing thresholds.

Cohen's parameters were considered when interpreting correlation values: between 0.10 and 0.29 indicate no or weak correlation, values between 0.30 and 0.49 indicate that there is moderate correlation and values between 0.50 and 1 can be interpreted as signs of strong correlation[15].

The significance level was set at 5% ($p \leq 0.05$), and data were analyzed in Jamovi software, version 2.3.21.

Results

Characterization of the sample

The sample had 77 adults – 41 of them in the COVID-19 group, of whom 68.3% were females (n = 28), and 31.7% were males (n = 13); and 36 in the control group, of whom 63.9% were females (n = 23), and 36.1% were males (n = 13). The mean age was 26.3 (± 8.01) years in the COVID-19 group and 25.8 (± 8.28) in the control group.

All individuals in the COVID-19 group were symptomatic. They were assessed 3 months after the disease, and the most frequent symptoms during the disease are described in Table 1.

All participants' audiological examination results and comparisons are described according to each procedure.

Table 1. Symptoms reported by the COVID-19 group (n = 42)

Symptoms	Yes (%)
Fever	47.61
Lack of taste	40.47
Lack of smell	40.47
Cough	38.09
Headache	30.95
Runny nose	28.57
Tiredness	23.8
Sore throat	19.04
Body ache	16.66
Diarrhea	11.9
Tinnitus	11.9
Shortness of breath	9.52
Hair loss	7.14
Chest pain	4.76
Nausea	2.38
Excessive hunger	2.38
Excessive sleepiness	2.38
Increased tongue size	2.38
Bloody stools	2.38
Affected memory	2.38
Intense ear pressure	2.38
Aural fullness	2.38
Muscle mass loss	2.38
Breathing difficulties	2.38
Chills	2.38
Malaise	2.38
Sinusitis	2.38
Heartburn	2.38

Acoustic immittance measures

All participants in both groups (n = 77) had type A tympanograms in both ears, and most of them had acoustic reflexes, both ipsilaterally and contralaterally.

PTA

All individuals (n = 77) had air-conduction hearing thresholds ≤ 25 dBHL at 250 to 8000 Hz, in both ears.

PTA verified a statistically significant difference in right-ear air-conduction hearing thresholds between the COVID-19 and control groups at 1000 Hz ($p = 0.017$), 2000 Hz ($p = 0.027$), and 3000 Hz ($p = 0.013$), with higher thresholds in the COVID-19 group. The exception was 8000 Hz, at which this group had significantly lower hearing thresholds ($p = 0.041$) (Table 2).

Table 2. Descriptive measures and comparison of both ears' air-conduction hearing thresholds in dBHL with the pure-tone threshold audiometry at 250 to 8000 Hz between the COVID-19 and control groups

Ear	Frequency (Hz)	Groups	Mean ± SD	Median	Q1-Q3	p-value
Right	250	COVID-19	3.66 ±6.62	5	0 – 10	0.388
		Control	5.69 ± 8.12	5		0 – 11.3
	500	COVID-19	5.85 ±5.80	5	0 – 10	0.235
		Control	4.58 ±7.11	5		0 – 6.25
	1000	COVID-19	6.46 ±6.25	5	5 – 10	0.017**
		Control	3.06 ±6.13	5		0 – 5
	2000	COVID-19	5.73 ±6.48	5	0 – 10	0.027**
		Control	2.36 ±5.79	0		0 – 6.25
	3000	COVID-19	7.68 ±6.90	5	5 – 10	0.014**
		Control	3.61 ±5.29	5		0 – 6.25
	4000	COVID-19	3.54 ±8.53	5	0 – 10	0.646
		Control	2.22 ±5.79	2.5		-1.25 – 5
	6000	COVID-19	2.80 ±7.42	5	-5 – 10	0.573
		Control	3.89 ±7.08	0		0 – 6.25
	8000	COVID-19	0.85 ±7.41	0	-5 – 5	0.022**
		Control	5.14 ±7.88	5		0 – 10
Left	250	COVID-19	3.66 ±6.80	5	0 – 5	0.200
		Control	5.83 ±7.32	5		0 – 10
	500	COVID-19	5.73 ±7.21	5	0 – 10	0.780
		Control	5.00 ±6.55	5		0 – 10
	1000	COVID-19	5.85 ±7.15	5	0 – 10	0.053
		Control	2.50 ±6.60	2.5		-5 – 5
	2000	COVID-19	5.85 ±7.15	5	0 – 10	0.147
		Control	3.89 ±5.99	5		0 – 5
	3000	COVID-19	8.05 ±8.68	5	0 – 15	0.108
		Control	4.31 ±5.37	5		0 – 10
	4000	COVID-19	5.12 ±8.33	5	0 – 10	0.170
		Control	2.50 ±6.15	2.5		0 – 5
	6000	COVID-19	3.05 ±7.90	5	-5 – 5	0.622
		Control	4.03 ±6.53	0		0 – 6.25
	8000	COVID-19	3.90 ±9.19	0	0 – 5	0.583
		Control	5.00 ±8.54	5		0 – 10

Caption: Hz = Hertz; SD = standard deviation, Q1 = quartile 1; Q3 = quartile 3; ** significant

The comparison of PTA air-conduction thresholds in the left ear between the two groups showed no statistically significant difference at 250 to 8000 Hz (Table 2).

TEOAE

All individuals in the control group had a response in both ears. In the COVID-19 group, it was absent unilaterally in two individuals (one on the right and the other on the left).

The COVID-19 group had a smaller TEOAE response amplitude than the control group, with a statistically significant difference at 1500 Hz ($p = 0.046$) in the right ear, whereas in the left one, there was no difference in response amplitude (Table 3).

A significant negative correlation was found between TEOAE and PTA findings at 1000 and 3000 Hz on the right ear and 1000, 2000, and 3000 Hz on the left ear – the smaller the TEOAE response amplitude, the higher the PTA air-conduction hearing threshold (Spearman correlation) (Figure 1).

Table 3. Descriptive measures and comparison of both ears' TEOAE response amplitudes between the COVID-19 (n=41) and control (n=36) groups.

Ear	Frequency (Hz)	Groups	Mean (±SD)	Median	Q1-Q3	p-value
Right	1000	COVID-19	11.0 (±5.83)	10.8	6.22-14.6	0.129
		Control	13.0 (±5.61)	13.2	9.13-15.2	
	1500	COVID-19	14.2 (±6.72)	15.2	8.99-18.4	0.046**
		Control	16.9 (±5.60)	17.7	13.5-20.7	
	2000	COVID-19	14.1 (±6.51)	13.9	9.05-18.5	0.183
		Control	16.3 (±5.68)	16.2	12.2-19.1	
	3000	COVID-19	16.5 (±6.85)	16.5	12.9-20.9	0.394
		Control	18.3 (±6.74)	20.6	11.7-24.6	
	4000	COVID-19	11.5 (±5.85)	11.2	6.85-15.5	0.909
		Control	11.5 (±6.19)	12.0	6.04-15.2	
Left	1000	COVID-19	11.9 (±6.05)	10.7	7.61-16.7	0.059
		Control	14.7 (±5.20)	15.0	10.5-17.5	
	1500	COVID-19	14.3 (±6.30)	13.5	10.6-18.3	0.190
		Control	16.2 (±6.15)	16.5	12.3-21.3	
	2000	COVID-19	13.6 (±6.16)	13.9	11.0-17.2	0.058
		Control	15.8 (±5.03)	16.2	13.6-19.9	
	3000	COVID-19	16.9 (±7.00)	18.3	11.7-21.7	0.496
		Control	18.3 (±5.74)	17.3	14.5-22.5	
	4000	COVID-19	11.3 (±6.45)	11.1	5.93-17.4	0.685
		Control	12.1 (±6.30)	11.0	6.75-17.4	

Caption: TEOAE = transient evoked otoacoustic emissions, Hz = Hertz; SD = standard deviation, Q1 = quartile 1; Q3 = quartile 3; ** significant

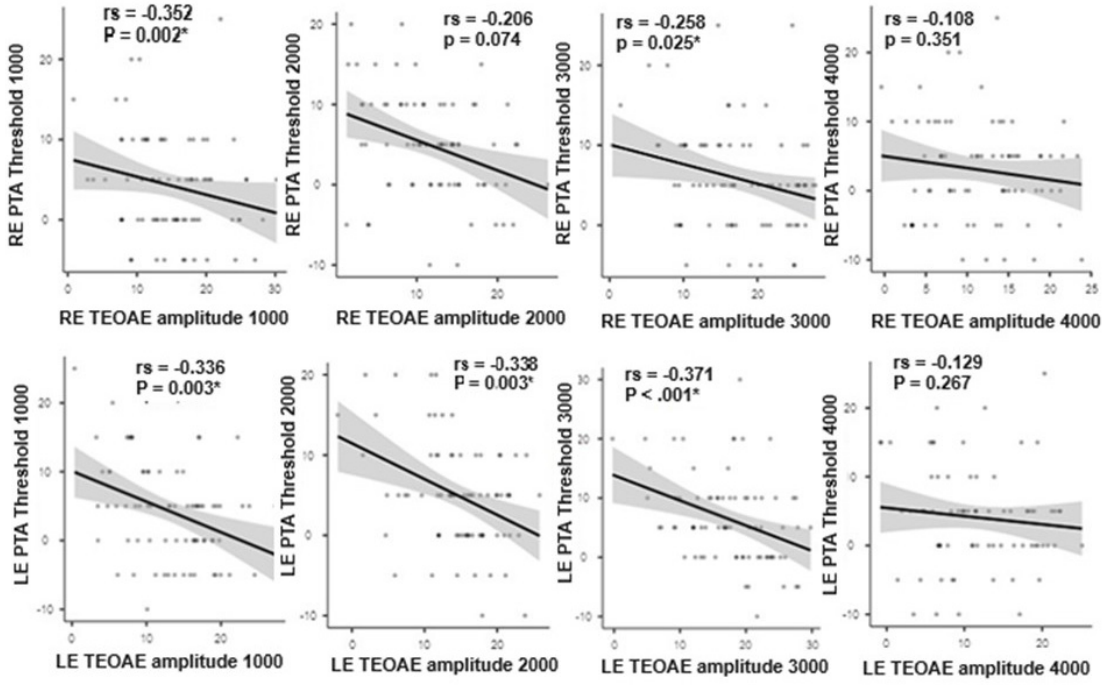

Figure 1. Correlation between PTA auditory thresholds and TEOAE response amplitudes at 500, 1000, 2000, and 4000 Hz in both ears (Spearman Correlation)

ABR

In this examination, when comparing the values obtained from the absolute latencies of waves I, III, and V and interpeak intervals I - III, III – V, and I - V, higher values of absolute and interpeak latencies were found for the COVID-19 group. This difference was statistically significant only for the absolute latency of wave I (p = 0.016) on the left ear (Table 4).

Table 4. Descriptive measures and comparison of both ears' absolute and interpeak latencies of ABR response between the COVID-19 and control groups.

Ear	Waves and interpeak intervals	Groups	Mean (±SD)	Median	Q1-Q3	p-value
Right	Wave I	COVID-19	1.69 (±0.13)	1.68	1.60-1.80	0.102
		Control	1.64 (±0.12)	1.64	1.55-1.73	
	Wave III	COVID-19	3.82 (±0.16)	3.80	3.73-3.90	0.405
		Control	3.78 (±0.15)	3.79	3.67-3.90	
	Wave V	COVID-19	5.73 (±0.21)	5.70	5.60-5.93	0.285
		Control	5.68 (±0.18)	5.68	5.58-5.84	
	Interpeak interval I - III	COVID-19	2.12 (±0.17)	2.15	2.05-2.22	0.980
		Control	2.14 (±0.13)	2.13	2.04-2.23	
	Interpeak interval III - V	COVID-19	1.91 (±0.14)	1.90	1.82-2.00	0.898
		Control	1.90 (±0.13)	1.92	1.81-1.99	
	Interpeak interval I - V	COVID-19	4.04 (±0.20)	4.00	3.88-4.15	0.822
		Control	3.98 (±0.43)	4.05	3.93-4.13	
Left	Wave I	COVID-19	1.67 (±0.13)	1.65	1.60-1.73	0.032**
		Control	1.60 (±0.10)	1.59	1.53-1.68	
	Wave III	COVID-19	3.84 (±0.21)	3.80	3.73-3.90	0.376
		Control	3.78 (±0.16)	3.79	3.65-3.91	
	Wave V	COVID-19	5.72 (±0.21)	5.68	5.60-5.83	0.306
		Control	5.65 (±0.19)	5.67	5.54-5.76	
	Interpeak interval I - III	COVID-19	2.17 (±0.17)	2.15	2.08-2.25	0.846
		Control	2.17 (±0.15)	2.17	2.10-2.26	
	Interpeak interval III - V	COVID-19	1.89 (±0.15)	1.90	1.80-1.98	0.533
		Control	1.87 (±0.14)	1.84	1.77-1.95	
	Interpeak interval I - V	COVID-19	4.06 (±0.20)	4.00	3.93-4.15	0.862
		Control	4.04 (±0.16)	4.04	3.95-4.18	

Caption: ABR = auditory brainstem response, DP = standard deviation, Q1 = quartile 1; Q3 = quartile 3; **significant

Discussion

The findings of this study demonstrate that there was an impact of COVID-19 on the auditory pathway to the brainstem, differently, according to the different tests carried out, the results of which will be discussed separately.

The first studies on a possible relationship between contamination by SARS-CoV-2 and the consequent hearing loss occurred in 2020[16,17].

One case of unilateral conductive hearing loss on the right side after SARS-CoV-2 infection and two other cases were reported, one with sensorineural alteration and the other with brain stem involvement16,17. These findings reinforce the need to investigate whether these changes can truly be attributed to infection by the virus in question[16,17].

Regarding the presence of clinical symptoms, the prevalence of contamination traits that appear most described in the literature were: tiredness, cough, shortness of breath, loss of smell and taste and headache[18]. In the present study, the most reported symptoms were fever, loss of smell and taste, cough, headache, and fatigue. As the symptoms correlate between studies, these manifestations are characteristic and recurrent in relation to contamination by the virus.

Based on the available data, it can be stated that the region where the collection was carried out had one of the lowest COVID-19 fatality rates in the country, with 70.5 and 79.4 deaths per 100 thousand inhabitants[19]. Furthermore, the most frequently encountered symptoms were those associated with the respiratory system, followed by gastrointestinal symptoms[20].

A recent review study detected several changes in the sensory system in post-COVID-19 syndrome, among which persistent auditory changes and the presence of tinnitus stand out3. However, in contrast to this study, no individual was found to have decreased hearing capacity, symptoms such as tinnitus were reported in a proportion of 11.9% and aural fullness was reported in 2.38% of the sample.

Regarding the investigation of auditory acuity, the PTA findings showed that airway auditory thresholds were significantly increased in the COVID-19 group for the frequencies of 1000, 2000 and 3000 Hz in the right ear in relation to the group's auditory thresholds. control, even though the values were within normal limits, for frequencies of 8000 Hz the hearing threshold was lower for the infected group.

Another researcher reinforced these findings, such as Mustafa21, who also did not find hearing loss in his series but observed statistically significant differences in the PTA airway auditory thresholds, at frequencies of 4000, 6000 and 8000 Hz, in 20 adults asymptomatic for COVID- 19 without complaints of hearing impairment.

Little is known about the pathophysiology of increased auditory thresholds in infected individuals. However, there are many ways in which the virus can affect the auditory system[4,5]. It has been demonstrated that the virus can cause inflammation and affect many organs, binding its spike (S) protein to the angiotensin-converting enzyme (ACE2) receptor present in several tissues, including the cochlea, cochlear nerve and central nervous system4,5. Furthermore, the virus that causes COVID-19 deoxygenates erythrocytes, which can lead to permanent hearing damage due to lack of oxygenation[3,4]. Another important hypothesis is endothelial dysfunction and microthrombi caused by COVID-19 infection, which probably reduce the ability to hear, causing a decrease in blood supply and contributing to the emergence of hearing loss[22].

It is also reported that the damage to hearing resulting from contamination by the SARS-CoV-2 virus may be related to damage to auditory structures due to an immune response to the virus, reaching such structures through blood vessels, nerves and even meninges[23,24].

Thus, these changes can reduce the motility of cochlear hair cells or even cell apoptosis, impacting performance in the TEOAE exam and consequently a lower response amplitude may be associated with greater latencies of ABR waves, indicating worse cochlear function. and a lower efficiency of nervous transmission[25].

Thus, in more critical situations of infection, other findings were observed, such as significantly increased airway auditory thresholds in a group of 74 individuals, with an average age of 60 years, who had moderate symptoms of COVID-19 and no previous history of hearing changes, when compared to the control group[26].

However, although the hearing change was not clinically identified through PTA, the findings of the present study indicate the need for auditory monitoring of individuals affected by COVID-19, to identify possible long-term hearing changes early, as there are reports in the literature that this infection can cause subclinical hearing loss[27,28].

Regarding the integrity of the functionality of the outer hair cells, when comparing the TEOAE response amplitudes between the groups, a lower response amplitude at the frequency of 1500 Hz was observed only in the right ear in the group with COVID-19. Other studies also identified reduced performance in the TEOAE exam, in a group of 20 adult individuals asymptomatic for the disease[22] and another in 30 adults[29].

However, Yildiz[30] did not identify differences in TEOAE test performance in individuals who had COVID-19 in relation to the control group up to three months after contracting the disease.

There is a hypothesis that the virus enters the hair cells of the cochlea, which could explain the difference in performance in otoacoustic emissions[24]. The investigation of hearing by magnetic resonance imaging of ten individuals with sensorineural hearing loss, after performing PTA, showed that, in addition to damage to the inner ear, there was the presence of intralabyrinthine hemorrhage and bilateral cochlear inflammation[31].

The correlation analysis between the TEOAE and PTA findings showed that the smaller the TEOAE response amplitude, the higher the auditory thresholds in the PTA, the strength of the

correlation was weak at frequencies of 1000 and moderate at 3000 Hz in the right ear and was moderate at frequencies of 1000, 2000 and 3000 Hz in the left ear in individuals from the COVID-19 group, which highlights the importance of carrying out TEOAEs in these individuals to detect possible changes in the outer hair cell mechanism before deteriorating auditory thresholds.

Similarly, another study found a significant decrease in TEOAE amplitude at frequencies of 1500, 2000 and 4000 Hz and a significant increase in auditory thresholds between frequencies of 4000 and 14000 Hz, in a group of 30 individuals between 18 and 45 years old (infected with COVID-19) when compared to a group of 30 individuals aged between 18 and 30 years for the control group[29].

Thus, research states that COVID-19 increases inflammatory processes in the cochlea, which can also damage hair cells, especially those located in the basal portion of the cochlea[8,21].

Viral infections can also affect brain stem structures, as in the case of COVID-19, as it can cause histological changes in the brain stem, resulting in inflammation, consequently affecting its vascularization and leading to neurodegeneration[23,32].

In the ABR assessment, higher absolute and interpeak latency values were found for the COVID-19 group, but this difference was only statistically significant in the absolute latency of wave I on the left. However, in another study, they found a significant difference in absolute latencies I, III and V between a group of 30 young adult individuals (infected by the SARS-CoV-2 virus) and 30 individuals from the control group[29].

Despite the findings of the slight change found in the BAEP, a possible justification can be attributed to the fact that the studied population did not present major impairments related to the disease. Therefore, different results can be found when evaluating individuals who require more invasive interventions[28].

Finally, future investigations, through studies with longitudinal designs, are necessary in relation to the decrease in the functionality of outer hair cells and the delay in the time of emergence of the electrophysiological response of the vestibulocochlear nerve.

Conclusion

Hearing assessment in adult individuals symptomatic for COVID-19 revealed a significant impact of the diseases on auditory structures. We observed worse auditory thresholds in the PTA, at frequencies of 1000, 2000 and 3000 Hz for the right ear and a decrease in the response amplitude in TEOAE for the 1500 Hz frequency band, for the right ear. Furthermore, the smaller the TEOAE response amplitudes, the higher the auditory thresholds were for the frequencies of 1000 and 3000 Hz in the right ear and for 1000, 2000 and 3000 in the left ear. Furthermore, the increase in the absolute latency of wave I, of the BAEP, in the left ear stood out.

Comparisons of audiological assessment results with individuals not infected by the SARS-CoV-2 virus made it possible to verify that the auditory system was impacted by this disease, demonstrating that COVID-19 can influence the performance of auditory structures, especially the functioning of outer hair cells. of the cochlea. However, monitoring and carrying out studies with larger and probabilistic samples will allow us to corroborate the findings found in this study.

We highlight some limitations of the study, such as the impossibility of carrying out assessments during the disease period due to contagiousness. The evaluations were carried out three months after the positive result of the polymerase chain reaction test. Furthermore, patients' symptoms related to the auditory system were recorded in a self-reported manner, which may be associated with memory bias, which may have influenced the information obtained in the COVID-19 group.

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